One week after withdrawal of valGCV, she developed primary CMV infection with pp65 antigenemia (1200/250,000 leukocytes). Response to intravenous treatment with GCV was slow with persisting viral replication. A mutation of the viral phosphotransferase (UL97) was detected. CMV replication and viremia became undetectable after reduction of immunosuppression in combination with continuing valGCV treatment. The peripheral lymphocyte counts increased, but the patient developed visual disturbances. A diagnosis of severe bilateral CMV retinitis was made and a therapy with foscarnet and eventually cidofovir was initiated. Although CMV retinitis was controlled, 4 month later vitrectomy became necessary due to retinal detachment. CMV replication recurred to low but detectable (5629 c/ml). The frequency of IFNγ-producing CMV specific CD4+ and CD8+ T cells after stimulation in vitro with CMV lysate was 0.365% and 0.245%, with CMV pp65 peptide pools 0.19% and 0.085%, respectively. Remarkably, the IFNγ-response to CMV pp72 (IE1) was 0.235% in CD4+, but 4.675% in CD8+ T cells (Figure 1).

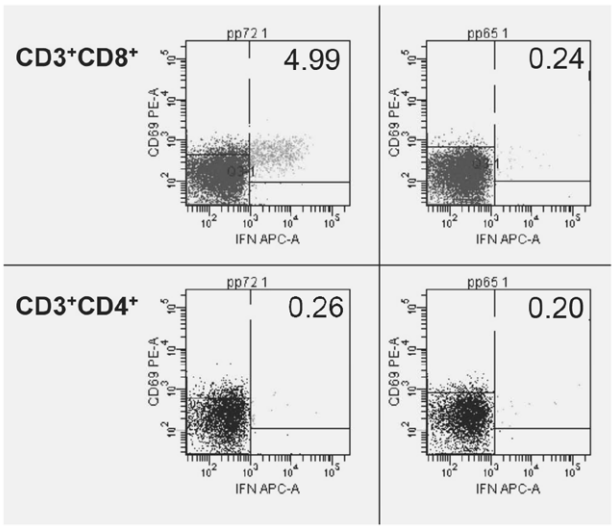

Fig. 1.

Conclusion: In this patient, the clinical signs of retinitis followed reduced immunosuppression, recovery of lymphocyte counts and the mounting of a highly selective pp72 CD8+ T cell response that was unmatched by a corresponding CD4+T-cell response. A prominent pp72 specific CD8+ T cell response without balancing CD4+ T-cells might provide an immunological correlate CMV-specific IRS. In such a situation, the use of steroids needs to be evaluated.

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Oral *Candida* Colonization in Solid Organ Transplant Recipients

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Background: Oral *Candida* colonization has been reported to be associated with a greater risk for esophagitis and pneumonitis in solid organ transplant recipients; however a systematic analysis of the oral *Candida* titers and species has not been previously conducted in this population. The objectives of this study were to determine the prevalence of oropharyngeal candidiasis and to define the oral carrier status, *Candida* titers and species in this population.
Methods: 63 kidney and heart transplant subjects were recruited from Hartford Hospital using the following criteria: 1. clinically stable; 2. at least one year post transplant; 3. no history of antifungal or antibiotic use within the last 4 months. Control subjects (n = 30) were age- and sex-matched, systemically healthy individuals. Subjects received an oral clinical examination. Swabs from the oral mucosa and a standardized amount of unstimulated saliva were plated on Chromagar® plates, and CFU/ml were calculated. Initial speciation was based on colony color and was confirmed by standard germination and biotyping (carbohydrate assimilation) assays.
Results: 1 of 63 transplant and 0 of 30 control subjects had oral infection with *C. albicans*. A significantly higher frequency of asymptomatic colonization was noted in transplant recipients (57.1%) compared to healthy controls (36.6%). In addition, the transplant group had significantly higher *Candida* titers than the control group. 83.3% of the transplant carriers were colonized by *C. albicans*, 16.6% by *C. glabrata* and 1% by *C. lusitaniae*. 22.2% of transplant carriers were colonized by more than one species, with the most frequent combination being *C. albicans* and *C. glabrata*. 81% of the control carriers were colonized by *C. albicans*, 0% by *C. glabrata* and 18% by *C. lusitaniae*. None of the control subjects were colonized by more than one species. The prevalence of xerostomia did not differ between test and control groups but the prevalence of diabetes was significantly higher in the transplant group.
Conclusions: Increased oral *Candida* carriage rate and titers were found in solid organ transplant subjects who are at least one year post-transplant. Although the majority of these subjects are colo-

nized by *C. albicans, C. glabrata* appears to emerge as the second most prevalent species.
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Pharmacokinetic and Pharmacodynamic Evaluation of Valganciclovir in Solid Organ Transplant Patients

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Goal: To validate oral valganciclovir (VGC) in the prophylaxis of CMV infection in lung (Lu) and liver (L) recipients and in the treatment of CMV infection/disease in solid organ transplant recipients, using pharmacokinetic and pharmacodynamic studies in comparison with i/v ganciclovir (GCV).
Methods: patients undergoing organ transplantation donor or recipient CMV-seropositive receiving VGC prophylaxis for a period of 3 months (D+/R- lung recipients, 6 months) were enrolled. Heart (H), Lu, and L recipients received 900 mg VGC q.d., adjusted to kidney (K) function. No K recipients received more than 450 mg of VGC q.d. GCV trough (Ctrough) and peak (Cpeak = 3 hours after drug administration) levels, and CMV DNA were measured at 7, 30, and 60 days post-transplant (prophylactic study). Patients who developed CMV infection/disease after stopping prophylaxis were treated with VGC (1800 mg per day adjusted to K function and GCV blood levels). GCV trough and peak levels, and CMV DNA were measured weekly for the first 3 weeks and biweekly thereafter, until therapy cessation (therapeutic study). Plasma concentration of GCV is measured by HPLC.
Results: In the first 8 prophylaxed patients (6 K, and 1 L and 1 H transplant recipient) of 450 mg VGC q.d., the average GCV concentration was 0.5±0.3 mg/l at trough, and 3.9±1.0 mg/l 3 hours after administration. Inter-patient variability was substantial, especially for Ctrough (63% of total variance), which correlated with the patient's estimated glomerular filtration rate (r square = 42%). No CMV DNA was detected during VGC prophylaxis. Two patients (1 H and 1 L) were treated for late CMV disease. Average GCV Cpeak were 8.9±2.3 mg/l and 4.6±0.5 mg/l, and GCV Ctrough were 2.0±0.9 mg/l and 1.6±0.2 mg/l respectively in each patient during induction phase. VGC treatment afforded a decrease in CMV DNA from 5.2 and 4.4 Log copies/10E6 cellules at week 0, to 3.9 and 3.0 at week 1, and 3.3 and 2.1 at week 3, respectively.
Conclusion: by demonstrating that valganciclovir produces drug levels and viral responses similar to i/v ganciclovir, this approach is promising as a cost effective alternative to randomized controlled studies in validating an oral prodrug in new indications.

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Efficacy of Preemptive Treatment Strategy for *Cytomegalovirus* (CMV) High-risk (D+/R-) Renal Transplant Recipients

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Background: The optimal strategy for prevention of CMV disease following renal transplantation is a matter of debate. Prophylactic treatment may result in late CMV disease, whereas preemptive treatment warrants regular consultations with laboratory screening. At our center, a preemptive strategy is used for high-risk (D+/R-) while follow-up for intermediate (R+) or low risk (D-/R-) patients is based on clinical symptoms.
Objectives: The aim of this retrospective analysis was to study the occurrence of CMV-antigenemia, -viral syndrome and -organ disease in renal transplant recipients and to correlate their respective impact on graft function and length of hospitalization, respectively.
Methods: All patients receiving a renal transplant from 1/1998 to 12/2003 with a completed follow-up of 2 years were included. High risk patients (D+/R-, group 1) had pp65 surveillance tests at regular intervals. Antiviral therapy was initiated if antigenemia was detected. The outcome of high-risk patients was compared with intermediate-risk (R+, group 2), and low-risk (D-/R-, group 3) patients.
Results: A total of 363 patients were eligible, 69 (19%) were D+/R- (group 1), 230 (63%) were D+/R+ or D-/R+ (group 2) and 64 (18%) were D-/R- (group 3). The preemptive treatment strategy was used in 59 (84%) patients of group 1, 9 (4%) of group 2 and 2 (3%) of group 3. Prophylaxis with ganciclovir (?) was used in 6 (9%) patients of group 1, all remaining patients were followed clinically. Overall, 70 (20%) patients suffered from at least one CMV episode (antigenemia, viral syndrome, or end organ disease). In group 1, 43 (62%) patients experienced a CMV episode, 8 (19%) had viremia,